In the claims:

Please amend claims 83, 84-88, 91, 93, 95, 97, 99-103, 106, 108, 110, 112, 120, 122-127, 129-133, 135, 137-140.

Please cancel claims 90, 92, 94, 96, 98, 105, 107, 109, 111, 113, 128, 134, 136.

1-73. **Cancelled**

74. **(Previously presented)** A pharmaceutical composition for treating a disorder in which TNFα activity is detrimental comprising an isolated human antibody, or an antigen-binding portion thereof, that dissociates from human TNFα with a K_d of 1 x 10^{-8} M or less and a K_{off} rate constant of 1 x 10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1 x 10^{-7} M or less, and at least one additional therapeutic agent.

75. **(Previously presented)** The pharmaceutical composition of claim 74, wherein the isolated human antibody, or antigen-binding portion thereof, dissociates from human TNFα with a K_{off} rate constant of 5 x 10^{-4} s^{-1} or less.

76. **(Previously presented)** The pharmaceutical composition of claim 74, wherein the isolated human antibody, or antigen-binding portion thereof, dissociates from human TNFα with a K_{off} rate constant of 1 x 10^{-4} s^{-1} or less.

77. **(Previously presented)** The pharmaceutical composition of claim 74, wherein the isolated human antibody, or antigen-binding portion thereof, neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1 x 10^{-8} M or less.

78. **(Previously presented)** The pharmaceutical composition of claim 74, wherein the isolated human antibody, or antigen-binding portion thereof, neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1 x 10^{-9} M or less.

79. **(Previously presented)** The pharmaceutical composition of claim 74, wherein the isolated human antibody, or antigen-binding portion thereof, neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1 x 10^{-10} M or less.

80. **(Previously presented)** The pharmaceutical composition of claim 74, wherein the isolated human antibody, or antigen-binding portion thereof, is a recombinant antibody, or antigen-binding portion thereof.

81. **(Previously presented)** The pharmaceutical composition of claim 74, wherein the isolated human antibody, or antigen-binding portion thereof, inhibits human TNFα-induced expression of ELAM-1 on human umbilical vein endothelial cells.

82. **(Previously presented)** The pharmaceutical composition of claim 74, wherein the isolated human antibody, or antigen-binding portion thereof, is D2E7.

83. **(Currently amended)** The pharmaceutical composition of claim 74, wherein the additional therapeutic agent is selected from the group consisting of non-steroidal anti-inflammatory drugs, cytokine suppressive anti-inflammatory drugs, CDP-571/BAY-10-3356, cA2, 75 kdTNFR-IgG , 55 kdTNFR-IgG, IDEC-CE9.1/SB 210396, DAB 486-IL-2, DAB 389-IL-2, Anti-Tac, IL-4, IL-10, IL-4 agonists, IL-10 agonists, IL-1RA, TNF-bp/s-TNFR, S284, R973401, MK-966, Iloprost, methotrexate, thalidomide, leflunomide, tranexamic acid, T614, prostaglandin E1, Tenidap, Naproxen, Meloxicam, Piroxicam, Diclofenac, Indomethacin, Sulfasalazine, Azathioprine, ICE inhibitors, zap-70 inhibitors, lck inhibitors, VEGF inhibitors, VEGF-R inhibitors, ~~corticosteroids~~ corticosteroid anti-inflammatory drugs, TNF-convertase inhibitors, anti-IL-12 antibodies, interleukin-11, interleukin-13, interleukin-17 inhibitors, gold, penicillamine, chloroquine, hydroxychloroquine, chlorambucil, cyclophosphamide, cyclosporin, anti-thymocyte globulin, anti-CD4 antibodies, CD5-toxins, orally-administered collagen, lobenzarit disodium, Cytokine Regulating Agents HP228 and HP466, ICAM-1 antisense phosphorothioate oligodeoxynucleotides, soluble complement receptor 1, prednisone, orgotein, glycosaminoglycan polysulphate, minocycline, anti-IL2R antibodies, marine lipids, botanical lipids, auranofin, phenylbutazone, meclofenamic acid, flufenamic acid, zileuton, mycophenolic

acid, tacrolimus, sirolimus, amiprilose, cladribine, azaribine, budenoside, epidermal growth factor, aminosalicylates, 6-mercaptopurine, metronidazole, lipoxygenase inhibitors, mesalamine, olsalazine, balsalazide, antioxidants, thromboxane inhibitors, IL-1 receptor antagonists, anti-IL-1β monoclonal antibodies, anti-IL-6 monoclonal antibodies, growth factors, elastase inhibitors, pyridinyl-imidazole compounds, glucuronide-conjugated prodrugs of prednisolone, dexamethasone or budesonide, dextran-conjugated prodrugs of prednisolone, dexamethasone or budesonide, soluble complement receptor 1, slow-release mesalazine, antagonists of Platelet Activating Factor (PAF), ciprofloxacin, lignocaine, prednisolone, methylprednisolone, cyclophosphamide, 4-aminopyridine, tizanidine, interferon-β1a, interferon-β1b, Copolymer 1, hyperbaric oxygen, intravenous immunoglobulin, clabribine, hypertonic saline solutions, antibiotics, continuous hemofiltration, carbapenems, antagonists of TNFα, antagonists of IL-1β, antagonists of IL-6 antagonists of IL-8, SK&F 107647, tetravalent guanylhydrazone CNI-1493, Tissue Factor Pathway Inhibitor, PHP, iron chelators and chelates, diethylenetriamine pentaacetic acid-iron (III) complex, lisofylline, PGG-Glucan, apolipoprotein A-1 reconstituted with lipids, chiral hydroxamic acids, anti-endotoxin antibodies, E5531, $rBPI_{21}$, Synthetic Anti-Endotoxin Peptides, surfactant replacement therapy and anti-IL-8 antibodies.

84. **(Currently amended)** A method for inhibiting human TNFα activity in a human subject suffering from a disorder in which TNFα activity is detrimental, comprising administering to the human subject an antibody and at least one additional therapeutic agent selected from the group consisting of a cytokine suppressive anti-inflammatory drug (CSAID), a non-steroidal anti-inflammatory drug (NSAID), a second antibody, a fusion protein, and an anti-inflammatory cytokine such that human TNFα activity is inhibited, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof, that dissociates from human TNFα with a K_d of 1×10^{-8} M or less and a K_{off} rate constant of 1×10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1×10^{-7} M or less.

85. **(Currently amended)** A method for inhibiting human TNFα activity in a human subject suffering from a disorder in which TNFα activity is detrimental, comprising

administering to the human subject an antibody and at least one additional therapeutic agent selected from the group consisting of a cytokine suppressive anti-inflammatory drug (CSAID), a non-steroidal anti-inflammatory drug (NSAID), a second antibody, a fusion protein, and an anti-inflammatory cytokine such that human TNFα activity is inhibited, wherein the antibody is an isolated human antibody, or antigen-binding portion thereof, with the following characteristics:

a) dissociates from human TNFα with a K_{off} rate constant of 1×10^{-3} s^{-1} or less, as determined by surface plasmon resonance,

b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;

c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12.

86. **(Currently amended)** A method for inhibiting human TNFα activity in a human subject suffering from a disorder in which TNFα activity is detrimental, comprising administering to the human subject an antibody and at least one additional therapeutic agent selected from the group consisting of a cytokine suppressive anti-inflammatory drug (CSAID), a non-steroidal anti-inflammatory drug (NSAID), a second antibody, a fusion protein, and an anti-inflammatory cytokine such that human TNFα activity is inhibited, wherein the antibody is an isolated human antibody, or an antigen binding portion thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2.

87. **(Currently amended)** A method for inhibiting human TNFα activity in a human subject suffering from a disorder in which TNFα activity is detrimental, comprising administering to the human subject an antibody and at least one additional therapeutic agent selected from the group consisting of a cytokine suppressive anti-inflammatory drug (CSAID), a non-steroidal anti-inflammatory drug (NSAID), a second antibody, a fusion protein, and an anti-

inflammatory cytokine such that human TNFα activity is inhibited, wherein the antibody is D2E7.

88. **(Currently amended)** The method of ~~any one of claims~~ claim 84, wherein the second antibody ~~additional therapeutic agent~~ is selected from the group consisting of ~~cytokine suppressive anti-inflammatory drugs,~~ CDP-57111/BAY-10-3356, cA2, ~~75 kdTNFR-IgG, 55 kdTNFR-IgG~~, IDEC-CE9.1/SB 210396, ~~DAB 486-IL-2, DAB 389-IL-2~~, Anti-Tac, IL-4 agonist antibody, IL-10 agonist antibody, an anti-CD4 antibody, anti-IL-1β monoclonal antibody, anti-IL-6 monoclonal antibody, anti-IL-8 antibody, anti-IL-12 antibody, and an anti-IL2R antibody. ~~IL-4 agonists, IL-10 agonists, IL-1RA, TNF bp/s-TNFR, S284, R973401, MK-966, Iloprost,~~

89. **(Previously presented)** The method of any one of claims 84, 85, 86, or 87, wherein the disorder is rheumatoid arthritis.

90. **Cancel**

91. **(Currently amended)** The method of ~~any one of claims~~ claim 84, wherein the disorder is inflammatory bowel disease.

92. **Cancel**

93. **(Currently amended)** The method of ~~any one of claims~~ claim 84, wherein the disorder is multiple sclerosis.

94. **Cancel**

95. **(Currently amended)** The method of ~~any one of claims~~ claim 84, wherein the disorder is sepsis.

96. **Cancel**

97. **(Currently amended)** The method of ~~any one of claims~~ claim 84, wherein the disorder is adult respiratory distress syndrome (ARDS).

98. **Cancel**

99. **(Currently amended)** A method for treating a subject suffering from a disorder in which TNFα activity is detrimental, comprising administering to the subject an antibody and at least one additional therapeutic agent selected from the group consisting of a cytokine suppressive anti-inflammatory drug (CSAID), a non-steroidal anti-inflammatory drug (NSAID), a second antibody, a fusion protein, and an anti-inflammatory cytokine, such that the disorder is treated, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof, that dissociates from human TNFα with a K_d of 1×10^{-8} M or less and a K_{off} rate constant of 1×10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1×10^{-7} M or less.

100. **(Currently amended)** A method for treating a subject suffering from a disorder in which TNFα activity is detrimental, comprising administering to the subject an antibody and at least one additional therapeutic agent selected from the group consisting of a cytokine suppressive anti-inflammatory drug (CSAID), a non-steroidal anti-inflammatory drug (NSAID), a second antibody, a fusion protein, and an anti-inflammatory cytokine, such that the disorder is treated, wherein the antibody is an isolated human antibody, or antigen-binding portion thereof, with the following characteristics:

a) dissociates from human TNFα with a K_{off} rate constant of 1×10^{-3} s^{-1} or less, as determined by surface plasmon resonance;

b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;

c) has a heavy chain CDR3 domain comprising the amino acid sequence

of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12.

101. **(Currently amended)** A method for treating a subject suffering from a disorder in which TNFα activity is detrimental, comprising administering to the subject an antibody and at least one additional therapeutic agent selected from the group consisting of a cytokine suppressive anti-inflammatory drug (CSAID), a non-steroidal anti-inflammatory drug (NSAID), a second antibody, a fusion protein, and an anti-inflammatory cytokine, such that the disorder is treated, wherein the antibody is an isolated human antibody, or an antigen binding portion thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2.

102. **(Currently amended)** A method for treating a subject suffering from a disorder in which TNFα activity is detrimental, comprising administering to the subject an antibody and at least one additional therapeutic agent selected from the group consisting of a cytokine suppressive anti-inflammatory drug (CSAID), a non-steroidal anti-inflammatory drug (NSAID), a second antibody, a fusion protein, and an anti-inflammatory cytokine, such that the disorder is treated, wherein the antibody is D2E7.

103. **(Currently amended)** The method of ~~any one of claims~~ claim 99, wherein the second antibody ~~additional therapeutic agent~~ is selected from the group consisting of ~~cytokine suppressive anti-inflammatory drugs,~~ CDP-57111/BAY-10-3356, cA2, ~~75 kdTNFR-IgG, 55 kdTNFR IgG~~, IDEC-CE9.1/SB 210396, ~~DAB 486 IL-2, DAB 389 IL-2~~, Anti-Tac, IL-4 agonist antibody, IL-10 agonist antibody, an anti-CD4 antibody, anti-IL-1β monoclonal antibody, anti-IL-6 monoclonal antibody, anti-IL-8 antibody, anti-IL-12 antibody, and an anti-IL2R antibody. ~~IL-4 agonists, IL-10 agonists~~, ~~IL-1RA, TNF bp/s-TNFR, S284, R973401, MK-966, Iloprost,~~

104. **(Previously presented)** The method of any one of claims 99, 100, 101, or 102, wherein the disorder is rheumatoid arthritis.

105. **Cancel**

106. **(Currently amended)** The method of ~~any one of claims~~ claim 99, wherein the disorder is inflammatory bowel disease.

107. **Cancel**

108. **(Currently amended)** The method of ~~any one of claims~~ claim 99, wherein the disorder is multiple sclerosis.

109. **Cancel**

110. **(Currently amended)** The method of ~~any one of claims~~ claim 99, wherein the disorder is sepsis.

111. **Cancel**

112. **(Currently amended)** The method of ~~any one of claims~~ claim 99, wherein the disorder is adult respiratory distress syndrome (ARDS).

113. **Cancel**

114. **(Previously presented)** A method for inhibiting human TNFα activity in a human subject suffering from a disorder in which TNFα activity is detrimental, wherein the disorder is selected from the group consisting of periodontal disease, obesity, and radiation toxicity, comprising administering to the human subject an antibody such that human TNFα activity in the human subject is inhibited, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof, that dissociates from human TNFα with a K_d of 1×10^{-8} M

or less and a K_{off} rate constant of 1×10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1×10^{-7} M or less.

115. **(Previously presented)** A method for inhibiting human TNFα activity in a human subject suffering from a disorder in which TNFα activity is detrimental, wherein the disorder is selected from the group consisting of periodontal disease, obesity, and radiation toxicity, comprising administering to the human subject an antibody such that human TNFα activity in the human subject is inhibited, wherein the antibody is an isolated human antibody, or antigen-binding portion thereof, with the following characteristics:

a) dissociates from human TNFα with a K_{off} rate constant of 1×10^{-3} s^{-1} or less, as determined by surface plasmon resonance;

b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;

c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12.

116. **(Previously presented)** A method for inhibiting human TNFα activity in a human subject suffering from a disorder in which TNFα activity is detrimental, wherein the disorder is selected from the group consisting of periodontal disease, obesity, and radiation toxicity, comprising administering to the human subject an antibody such that human TNFα activity in the human subject is inhibited, wherein the antibody is an isolated human antibody, or an antigen binding portion thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2.

117. **(Previously presented)** A method for inhibiting human TNFα activity in a human subject suffering from a disorder in which TNFα activity is detrimental, wherein the disorder is selected from the group consisting of periodontal disease, obesity, and radiation toxicity, comprising administering to the human subject an antibody such that human TNFα activity in the human subject is inhibited, wherein the antibody is D2E7.

118. **(Previously presented)** A method for treating a subject suffering from a disorder in which TNFα activity is detrimental, wherein the disorder is selected from the group consisting of periodontal disease, obesity, and radiation toxicity, comprising administering to the subject an antibody such that the disorder is treated, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof, that dissociates from human TNFα with a k_d of 1×10^{-8} m or less and a k_{off} rate constant of 1×10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1×10^{-7} m or less.

119. **(Previously presented)** A method for treating a subject suffering from a disorder in which TNFα activity is detrimental, wherein the disorder is selected from the group consisting of periodontal disease, obesity, and radiation toxicity, comprising administering to the subject an antibody such that the disorder is treated, wherein the antibody is an isolated human antibody, or antigen-binding portion thereof, with the following characteristics:

a) dissociates from human TNFα with a K_{off} rate constant of 1×10^{-3} s^{-1} or less, as determined by surface plasmon resonance;

b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;

c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12.

120. **(Currently amended)** A method for treating a subject suffering from a disorder in which TNFα activity is detrimental, wherein the disorder is selected from the group consisting of periodontal disease, obesity, and radiation toxicity, comprising administering to the subject an antibody such that the disorder is treated, wherein the antibody is an isolated human antibody, or an antigen binding portion thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2.

121. **(Previously presented)** A method for treating a subject suffering from a disorder in which TNFα activity is detrimental, wherein the disorder is selected from the group consisting of periodontal disease, obesity, and radiation toxicity, comprising administering to the subject an antibody such that the disorder is treated, wherein the antibody is D2E7.

122. **(Currently amended)** The method of claim 118, wherein ~~the additional therapeutic agent~~ the isolated human antibody is administered with at least one additional therapeutic agent ~~is~~ selected from the group consisting of non-steroidal anti-inflammatory drugs, cytokine suppressive anti-inflammatory drugs, CDP-571/BAY-10-3356, cA2, 75 kdTNFR-IgG , 55 kdTNFR-IgG, IDEC-CE9.1/SB 210396, DAB 486-IL-2, DAB 389-IL-2, Anti-Tac, IL-4, IL-10, IL-4 agonists, IL-10 agonists, IL-1RA, TNF-bp/s-TNFR, S284, R973401, MK-966, Iloprost, methotrexate, thalidomide, leflunomide, tranexamic acid, T614, prostaglandin E1, Tenidap, Naproxen, Meloxicam, Piroxicam, Diclofenac, Indomethacin, Sulfasalazine, Azathioprine, ICE inhibitors, zap-70 inhibitors, lck inhibitors, VEGF inhibitors, VEGF-R inhibitors, ~~corticosteroids~~ corticosteroid anti-inflammatory drugs, TNF-convertase inhibitors, anti-IL-12 antibodies, interleukin-11, interleukin-13, interleukin-17 inhibitors, gold, penicillamine, chloroquine, hydroxychloroquine, chlorambucil, cyclophosphamide, cyclosporin, anti-thymocyte globulin, anti-CD4 antibodies, CD5-toxins, orally-administered collagen, lobenzarit disodium, Cytokine Regulating Agents HP228 and HP466, ICAM-1 antisense phosphorothioate oligodeoxynucleotides, soluble complement receptor 1, prednisone, orgotein, glycosaminoglycan polysulphate, minocycline, anti-IL2R antibodies, marine lipids, botanical lipids, auranofin, phenylbutazone, meclofenamic acid, flufenamic acid, zileuton, mycophenolic acid, tacrolimus, sirolimus, amiprilose, cladribine, azaribine, budenoside, epidermal growth

factor, aminosalicylates, 6-mercaptopurine, metronidazole, lipoxygenase inhibitors, mesalamine, olsalazine, balsalazide, antioxidants, thromboxane inhibitors, IL-1 receptor antagonists, anti-IL-1β monoclonal antibodies, anti-IL-6 monoclonal antibodies, growth factors, elastase inhibitors, pyridinyl-imidazole compounds, glucuronide-conjugated prodrugs of prednisolone, dexamethasone or budesonide, dextran-conjugated prodrugs of prednisolone, dexamethasone or budesonide, soluble complement receptor 1, slow-release mesalazine, antagonists of Platelet Activating Factor (PAF), ciprofloxacin, lignocaine, prednisolone, methylprednisolone, cyclophosphamide, 4-aminopyridine, tizanidine, interferon-β1a, interferon-β1b, Copolymer 1, hyperbaric oxygen, intravenous immunoglobulin, clabribine, hypertonic saline solutions, antibiotics, continuous hemofiltration, carbapenems, antagonists of TNFα, antagonists of IL-1β, antagonists of IL-6 antagonists of IL-8, SK&F 107647, tetravalent guanylhydrazone CNI-1493, Tissue Factor Pathway Inhibitor, PHP, iron chelators and chelates, diethylenetriamine pentaacetic acid-iron (III) complex, lisofylline, PGG-Glucan, apolipoprotein A-1 reconstituted with lipids, chiral hydroxamic acids, anti-endotoxin antibodies, E5531, $rBPI_{21}$, Synthetic Anti-Endotoxin Peptides, surfactant replacement therapy and anti-IL-8 antibodies.

123. **(Currently amended)** The method of claim 84, wherein the CSAID ~~additional therapeutic agent~~ is either ~~selected from the group consisting of methotrexate, an IL-12 antibody,~~ leflunomide or T-614. ~~, Naproxen, Diclofenac, Sulfasalazine, chloroquine, hydroxychloroquine, non-steroidal anti-inflammatory drugs, prednisone, prednisolone, methylprednisolone, and gold.~~

124. **(Currently amended)** The method of claim 84, wherein the NSAID ~~additional therapeutic agent~~ is selected from the group consisting of ~~thalidomide, tranexamic acid, T-614, prostaglandin E1,~~ tenidap, naproxen, meloxicam, Diclofenac, ibuprofen, piroxicam, indomethacin, and leflunomide. ~~azathioprine, ICE inhibitors, zap-70 inhibitors, Ick inhibitors, VEGF inhibitors, VEGF-R inhibitors, corticosteroids, and TNF-convertase inhibitors.~~

125. **(Currently amended)** The method of claim 84, wherein the anti-inflammatory cytokine ~~additional therapeutic agent~~ is selected from the group consisting of interleukin-11, interleukin-13, IL-4, and IL-10. ~~interleukin-17 inhibitors, penicillamine,~~

~~chloroquine, hydroxychloroquine, chlorambucil, cyclophosphamide, cyclosporin, anti-thymocyte globulin, anti-CD4 antibodies, CD5-toxins, orally-administered collagen, lobenzarit disodium, cytokine regulating agents HP228 and HP-466, ICAM-1 antisense phosphorothioate oligodeoxynucleotides, soluble complement receptor 1, orgotein, glycosaminoglycan polysulphate, minocycline, anti-IL2R antibodies, marine lipids, botanical lipids, auranofin, phenylbutazone, meclofenamic acid, and flufenamic acid~~.

126. **(Currently amended)** The method of claim 84, wherein the fusion protein ~~additional therapeutic agent~~ is selected from the group consisting of 75 kdTNFR-IgG, 55 kdTNFR-IgG, DAB 486-IL-2, and DAB 389-IL-2. ~~zileuton, mycophenolic acid, tacrolimus, sirolimus, amiprilose, cladribine, azaribine, budenoside, epidermal growth factor, aminosalicylates, 6-mercaptopurine, metronidazole, lipoxygenase inhibitors, mesalamine, olsalazine, balsalazide, antioxidants, thromboxane inhibitors, IL-1 receptor antagonists, anti-IL-1β monoclonal antibodies, anti-IL-6 monoclonal antibodies, growth factors, elastase inhibitors, pyridinyl-imidazole compounds, glucuronide-conjugated prodrugs of prednisolone, dexamethasone or budesonide, dextran-conjugated prodrugs of prednisolone, dexamethasone or budesonide, soluble complement receptor 1, slow-release mesalazine, antagonists of Platelet Activating Factor (PAF), ciprofloxacin, and lignocaine.~~

127. **(Currently amended)** The method of claim 84, A method for inhibiting human TNFα activity in a human subject suffering from a disorder in which TNFα activity is detrimental, comprising administering to the human subject an antibody and at least one additional therapeutic agent such that human TNFα activity is inhibited, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof, that dissociates from human TNFα with a Kd of 1 x 10-8 M or less and a Koff rate constant of 1 x 10-3 s-1 or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard in vitro L929 assay with an IC50 of 1 x 10-7 M or less, wherein the additional therapeutic agent is selected from the group consisting of cyclophosphamide, 4-aminopyridine, tizanidine, interferon-β1a, interferon-β1b, Copolymer 1, hyperbaric oxygen, intravenous immunoglobulin, clabribine, hypertonic saline solutions, antibiotics, continuous hemofiltration, carbapenems, antagonists of TNFα, antagonists of IL-1β, antagonists of IL-6 antagonists of IL-8,

SK&F 107647, tetravalent guanylhydrazone CNI-1493, Tissue Factor Pathway Inhibitor, PHP, iron chelators and chelates, diethylenetriamine pentaacetic acid-iron (III) complex, lisofylline, PGG-Glucan, apolipoprotein A-1 reconstituted with lipids, chiral hydroxamic acids, anti-endotoxin antibodies, E5531, rBPI21, Synthetic Anti-Endotoxin Peptides, surfactant replacement therapy, IL-4 agonists, IL-10 agonists, IL-1RA, TNF-bp/s-TNFR, S284, R973401, MK-966, Iloprost, methotrexate, sulfasalazine, chloroquine, hydroxychloroquine, non-steroidal anti-inflammatory drugs, prednisone, prednisolone, methylprednisolone, gold, thalidomide, tranexamic acid, prostaglandin E1, azathioprine, ICE inhibitors, zap-70 inhibitors, lck inhibitors, VEGF inhibitors, VEGF-R inhibitors, corticosteroid anti-inflammatory drugs, TNF-convertase inhibitors, interleukin-17 inhibitors, penicillamine, chlorambucil, cyclophosphamide, cyclosporin, anti-thymocyte globulin, CD5-toxins, lobenzarit disodium, cytokine regulating agents HP228 and HP 466, ICAM-1 antisense phosphorothioate oligodeoxynucleotides, soluble complement receptor 1, orgotein, glycosaminoglycan polysulphate, minocycline, marine lipids, botanical lipids, auranofin, phenylbutazone, meclofenamic acid, flufenamic acid, zileuton, mycophenolic acid, tacrolimus, sirolimus, amiprilose, azaribine, budenoside, epidermal growth factor, aminosalicylates, 6-mercaptopurine, metronidazole, lipoxygenase inhibitors, mesalamine, olsalazine, balsalazide, antioxidants, thromboxane inhibitors, growth factors, elastase inhibitors, pyridinyl-imidazole compounds, glucuronide-conjugated prodrugs of prednisolone, dexamethasone or budesonide, dextran-conjugated prodrugs of prednisolone, dexamethasone or budesonide, slow-release mesalazine, antagonists of Platelet Activating Factor (PAF), ciprofloxacin, and lignocaine. ~~anti-IL-8 antibodies.~~

128. **Cancel**

129. **(Currently amended)** The method of claim 99, wherein the CSAID ~~additional therapeutic agent~~ is either ~~selected from the group consisting of methotrexate, an IL-12 antibody~~, leflunomide or T-614. ~~Naproxen, Diclofenac, Sulfasalazine, chloroquine, hydroxychloroquine, non-steroidal anti-inflammatory drugs, prednisone, prednisolone, methylprednisolone, and gold~~.

130. **(Currently amended)** The method of claim 99, wherein the NSAID ~~additional therapeutic agent~~ is selected from the group consisting of ~~thalidomide, tranexamic acid, T-614, prostaglandin E1~~, tenidap, naproxen, meloxicam, Diclofenac, ibuprofen, piroxicam, indomethacin, and leflunomide. ~~azathioprine, ICE inhibitors, zap-70 inhibitors, Ick inhibitors, VEGF inhibitors, VEGF-R inhibitors, corticosteroids, and TNF-convertase inhibitors.~~

131. **(Currently amended)** The method of claim 99, wherein the anti-inflammatory cytokine ~~additional therapeutic agent~~ is selected from the group consisting of interleukin-11, interleukin-13, IL-4, and Il-10. ~~interleukin-17 inhibitors, penicillamine, chloroquine, hydroxychloroquine, chlorambucil, cyclophosphamide, cyclosporin, anti-thymocyte globulin, anti-CD4 antibodies, CD5-toxins, orally-administered collagen, lobenzarit disodium, cytokine regulating agents HP228 and HP-466, ICAM-1 antisense phosphorothioate oligodeoxynucleotides, soluble complement receptor-1, orgotein, glycosaminoglycan polysulphate, minocycline, anti-IL2R antibodies, marine lipids, botanical lipids, auranofin, phenylbutazone, meclofenamic acid, and flufenamic acid~~.

132. **(Currently amended)** The method of claim 99, wherein the fusion protein ~~additional therapeutic agent~~ is selected from the group consisting of 75 kdTNFR-IgG , 55 kdTNFR-IgG, DAB 486-IL-2, and DAB 389-IL-2. ~~zileuton, mycophenolic acid, tacrolimus, sirolimus, amiprilose, cladribine, azaribine, budenoside, epidermal growth factor, aminosalicylates, 6-mercaptopurine, metronidazole, lipoxygenase inhibitors, mesalamine, olsalazine, balsalazide, antioxidants, thromboxane inhibitors, IL-1 receptor antagonists, anti-IL-1β monoclonal antibodies, anti-IL-6 monoclonal antibodies, growth factors, elastase inhibitors, pyridinyl-imidazole compounds, glucuronide-conjugated prodrugs of prednisolone, dexamethasone or budesonide, dextran-conjugated prodrugs of prednisolone, dexamethasone or budesonide, soluble complement receptor-1, slow-release mesalazine, antagonists of Platelet Activating Factor (PAF), ciprofloxacin, and lignocaine~~.

133. **(Currently amended)** ~~The method of claim 99~~ A method for treating a subject suffering from a disorder in which TNFα activity is detrimental, comprising administering to the subject an antibody and at least one additional therapeutic agent, such that

the disorder is treated, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof, that dissociates from human TNFα with a K_d of 1 x 10^{-8} M or less and a K_{off} rate constant of 1 x 10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1 x 10^{-7} M or less, wherein the additional therapeutic agent is selected from the group consisting of cyclophosphamide, 4-aminopyridine, tizanidine, interferon-β1a, interferon-β1b, Copolymer 1, hyperbaric oxygen, intravenous immunoglobulin, clabribine, hypertonic saline solutions, antibiotics, continuous hemofiltration, carbapenems, antagonists of TNFα, antagonists of IL-1β, antagonists of IL-6 antagonists of IL-8, SK&F 107647, tetravalent guanylhydrazone CNI-1493, Tissue Factor Pathway Inhibitor, PHP, iron chelators and chelates, diethylenetriamine pentaacetic acid-iron (III) complex, lisofylline, PGG-Glucan, apolipoprotein A-1 reconstituted with lipids, chiral hydroxamic acids, anti-endotoxin antibodies, E5531, $rBPI_{21}$, Synthetic Anti-Endotoxin Peptides, surfactant replacement therapy, IL-4 agonists, IL-10 agonists, IL-1RA, TNF-bp/s-TNFR, S284, R973401, MK-966, Iloprost, methotrexate, sulfasalazine, chloroquine, hydroxychloroquine, non-steroidal anti-inflammatory drugs, prednisone, prednisolone, methylprednisolone, gold, thalidomide, tranexamic acid, prostaglandin E1, azathioprine, ICE inhibitors, zap-70 inhibitors, lck inhibitors, VEGF inhibitors, VEGF-R inhibitors, corticosteroid anti-inflammatory drugs, TNF-convertase inhibitors, interleukin-17 inhibitors, penicillamine, chlorambucil, cyclophosphamide, cyclosporin, anti-thymocyte globulin, CD5-toxins, lobenzarit disodium, cytokine regulating agents HP228 and HP 466, ICAM-1 antisense phosphorothioate oligodeoxynucleotides, soluble complement receptor 1, orgotein, glycosaminoglycan polysulphate, minocycline, marine lipids, botanical lipids, auranofin, phenylbutazone, meclofenamic acid, flufenamic acid, zileuton, mycophenolic acid, tacrolimus, sirolimus, amiprilose, azaribine, budenoside, epidermal growth factor, aminosalicylates, 6-mercaptopurine, metronidazole, lipoxygenase inhibitors, mesalamine, olsalazine, balsalazide, antioxidants, thromboxane inhibitors, growth factors, elastase inhibitors, pyridinyl-imidazole compounds, glucuronide-conjugated prodrugs of prednisolone, dexamethasone or budesonide, dextran-conjugated prodrugs of prednisolone, dexamethasone or budesonide, slow-release mesalazine, antagonists of Platelet Activating Factor (PAF), ciprofloxacin, and lignocaine. ~~anti-IL-8 antibodies~~.

134. **Cancel**

135. **(Currently amended)** A method for treating a subject suffering from rheumatoid arthritis, comprising administering to the subject an antibody and at least one additional therapeutic agent selected from the group consisting of methotrexate, an IL-12 antibody, leflunomide, Naproxen, Diclofenac, Sulfasalazine, chloroquine, hydroxychloroquine, non-steroidal anti-inflammatory drugs, prednisone, prednisolone, methylprednisolone, and gold, such that the rheumatoid arthritis is treated, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof, that dissociates from human TNFα with a K_d of 1 x 10^{-8} M or less and a K_{off} rate constant of 1 x 10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1 x 10^{-7} M or less.

136. **(Cancel)**

137. **(Currently amended)** A method for treating a subject suffering from rheumatoid arthritis, comprising administering to the subject an antibody and at least one additional therapeutic agent, such that the rheumatoid arthritis is treated, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof, that dissociates from human TNFα with a K_d of 1 x 10^{-8} M or less and a k_{off} rate constant of 1 x 10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1 x 10^{-7} M or less, ~~The method of claim 135,~~ wherein the wherein the additional therapeutic agent is selected from the group consisting of cytokine suppressive anti-inflammatory drugs, CDP-571/BAY-10-3356, cA2, 75 kdTNFR-IgG , 55 kdTNFR-IgG, IDEC-CE9.1/SB 210396, DAB 486-IL-2, DAB 389-IL-2, Anti-Tac, IL-4, IL-10, IL-4 agonists, IL-10 agonists, IL-1RA, TNF-bp/s-TNFR, S284, R973401, MK-966, Iloprost, thalidomide, tranexamic acid, T614, prostaglandin E1, Tenidap, Naproxen, Meloxicam, Piroxicam, Indomethacin, Azathioprine, ICE inhibitors, zap-70 inhibitors, Ick inhibitors, VEGF inhibitors, VEGF-R inhibitors, ~~corticosteroids~~ corticosteroid anti-inflammatory drugs, TNF-convertase inhibitors, anti-IL-12 antibodies, interleukin-11, interleukin-13, interleukin-17 inhibitors, penicillamine, chlorambucil, cyclophosphamide, cyclosporin, anti-thymocyte

globulin, anti-CD4 antibodies, CD5-toxins, orally-administered collagen, lobenzarit disodium, Cytokine Regulating Agents HP228 and HP466, ICAM-1 antisense phosphorothioate oligodeoxynucleotides, soluble complement receptor 1, orgotein, glycosaminoglycan polysulphate, minocycline, anti-IL2R antibodies, marine lipids, botanical lipids, auranofin, phenylbutazone, meclofenamic acid, flufenamic acid, intravenous immunoglobulin, zileuton, mycophenolic acid, tacrolimus, sirolimus, amiprilose, cladribine, and azaribine.

138. **(Currently amended)** A method for treating a subject suffering from rheumatoid arthritis, comprising administering to the subject an antibody and at least one additional therapeutic agent selected from the group consisting of methotrexate, an IL-12 antibody, leflunomide, naproxen, diclofenac, sulfasalazine, chloroquine, hydroxychloroquine, non-steroidal anti-inflammatory drugs, prednisone, prednisolone, methylprednisolone, and gold, such that the rheumatoid arthritis is treated, wherein the antibody is an isolated human antibody, or antigen-binding portion thereof, with the following characteristics:

a) dissociates from human TNFα with a K_{off} rate constant of 1×10^{-3} s^{-1} or less, as determined by surface plasmon resonance;

b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;

c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12.

139. **(Currently amended)** A method for treating a subject suffering from rheumatoid arthritis, comprising administering to the subject an antibody and at least one additional therapeutic agent selected from the group consisting of methotrexate, an IL-12 antibody, leflunomide, naproxen, diclofenac, sulfasalazine, chloroquine, hydroxychloroquine, non-steroidal anti-inflammatory drugs, prednisone, prednisolone, methylprednisolone, and gold, such that the rheumatoid arthritis is treated, wherein the antibody is an isolated human antibody, or an antigen binding portion thereof, with a light chain variable region (LCVR) comprising the

amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2.

140. **(Currently amended)** A method for treating a subject suffering from rheumatoid arthritis, comprising administering to the subject an antibody and at least one additional therapeutic agent selected from the group consisting of methotrexate, an IL-12 antibody, leflunomide, naproxen, diclofenac, sulfasalazine, chloroquine, hydroxychloroquine, non-steroidal anti-inflammatory drugs, prednisone, prednisolone, methylprednisolone, and gold such that the rheumatoid arthritis is treated, wherein the antibody is D2E7.

141. **(Previously presented)** A method for treating a subject suffering from rheumatoid arthritis, comprising administering to the subject an antibody and methotrexate, such that the rheumatoid arthritis is treated, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof, that dissociates from human TNFα with a K_d of 1 x 10^{-8} M or less and a K_{off} rate constant of 1 x 10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1 x 10^{-7} M or less.

142. **(Previously presented)** A method for treating a subject suffering from rheumatoid arthritis, comprising administering to the subject an antibody and methotrexate such that the rheumatoid arthritis is treated, wherein the antibody is D2E7.